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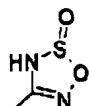
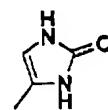
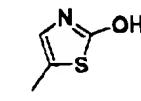
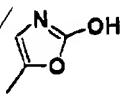
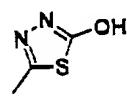
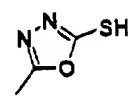
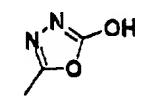
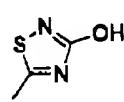
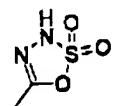
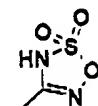
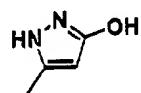
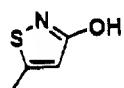
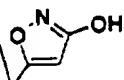
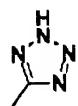
n is 0, 1 or 2;

m is 1 or 2;

X is S or O;

Y is O, S, SO or SO₂;

R₁ is selected from the group consisting of hydrogen, 5-membered heterocycles selected from the group consisting of:



COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl and COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₂ is hydrogen, C₁-C₆alkyl, hydroxy or NR₇R₈;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

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R₄, R₅ and R₆ are independently hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxy-carbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆-alkyl, thio, C₁-C₆alkylthio, C₁-C₆alkylthioC₁-C₆alkyl, arylthio, arylC₁-C₆alkyl-thio, arylC₁-C₆alkylthioC₁-C₆alkyl, NR₈R₉, C₁-C₆alkylaminoC₁-C₆alkyl, aryl-C₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkyl-carbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆-alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxy, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkyl-carboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₁, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below and R₇ is NR₈R₉, or C₁-C₆alkylNR₈R₉;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkyl-carboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined in the section of definitions; or R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, the ring system can optionally be substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, C₁-C₆alkyloxy, arylC₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino-C₁-C₆alkyl or NR₉R₁₀, wherein R₉ and R₁₀ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below; or R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam; wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo,

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COOR₃, CONR₇R₈, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, thio, C₁-C₆alkylthio, arylthio, arylC₁-C₆alkylthio, NR₇R₈, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkyl-carboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonyl-amino, -C₁-C₆alkylaminoCOR₁₂, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, -CONR₇R₈, -C₁-C₆alkylCONR₇R₈, or a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam, wherein R₁₂ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy; and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, COOR₃, CONR₇R₈, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, thio, C₁-C₆alkylthio, C₁-C₆alkylthioC₁-C₆alkyl, arylthio, arylC₁-C₆alkylthio, arylC₁-C₆alkylthioC₁-C₆alkyl, NR₇R₈, C₁-C₆-alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkyl-aminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkyl-carbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, carboxyC₁-C₆alkyloxy, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₁, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -CONR₇R₈, or -C₁-C₆alkylCONR₇R₈;

with the proviso that when R₁ is COOH, R₂, R₃, R₄, R₅, and R₆ are H, n and m are 1, and X is S, then Y is not O, S, SO or SO₂;

when R₂, R₃, R₄, R₅, and R₆ are H, n and m are 1, X is S, and Y is O, then R₁ is not 5-tetrazol;

when R₁ is COOH, R₂, R₃, R₄, R₅, and R₆ are H, n and m are 1, X is S, and Y is O, then R₃ is not 5-tetrazol;

when R₁ is COOH, R₂, R₃, R₄, and R₆ are H, n and m is 1, X is S and Y is O, then R₅ is not 1-oxo-1,3-dihydro-isoindol-2-yl methyl, 1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl, ((4-oxo-chromene-4H-3-carbonyl)amino)methyl, 1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl, ((4-oxo-

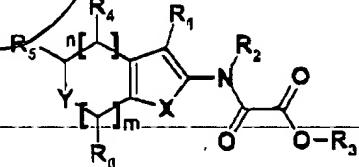
chromene-4H-3-carbonyl)amino)methyl, ((4-oxo-chromene-4H-2-carbonyl)amino)methyl, (3-furan-3-yl-acryloylomino)methyl, (3-furan-2-yl-acryloylamino)-methyl, ((3-oxo-indane-1-carbonyl)amino)methyl, 2,4-dioxo-thiazolidin-3-ylmethyl, 3,5-dimethoxy-benzoylamino-methyl, 5,6-dichloro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl, 1,3-dioxo-1,3,4,5,6,7-hexahydro-isoindol-2-ylmethyl, 1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl, (4-methoxy-benzenesulfonylamino)-methyl, 2-methyl-4-oxo-4H-quinazolin-3-ylmethyl, or 1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl;

when R₁ is COOH, R₂, R₃, R₄, and R₅ are H, n and m are 1, X is S, and Y is O, then R₆ is not 1,3,-dioxo-1,3-dihydro-isoindol-2-ylmethyl or acetylamino-methyl;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

2. (Amended)

A compound of Formula 1



Formula 1

wherein

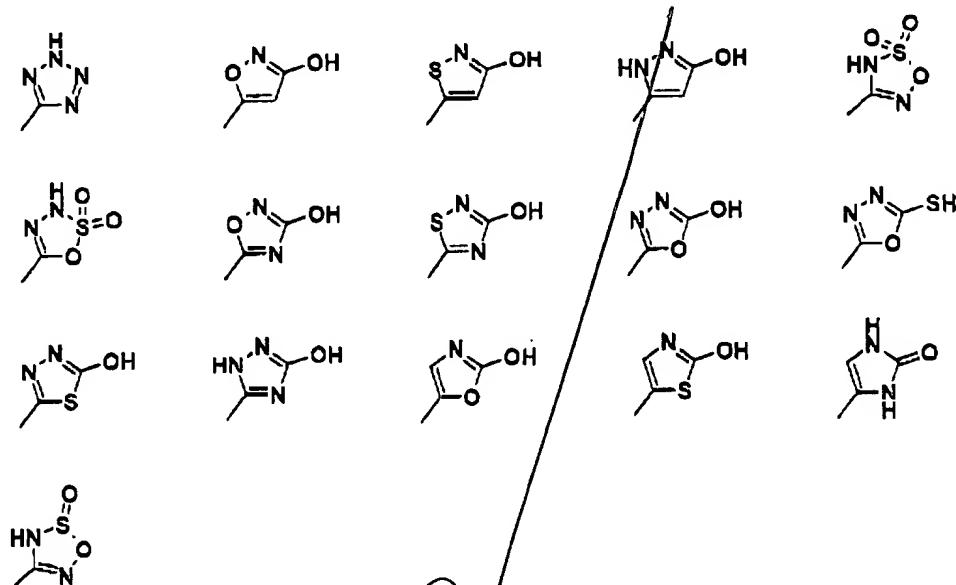
n is 0, 1 or 2;

m is 1 or 2;

X is S or O;

Y is O, S, SO or SO₂;

R₁ is selected from the group consisting of hydrogen, 5-membered heterocycles selected from the group consisting of:



COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl and
COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₂ is hydrogen, C₁-C₆alkyl, hydroxy or NR₇R₈;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄, R₅ and R₆ are independently hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxy-carbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, thio, C₁-C₆alkyl-thio, C₁-C₆alkylthioC₁-C₆alkyl, arylthio, arylC₁-C₆alkyl-thio, arylC₁-C₆alkylthioC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, aryl-C₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkyl-carbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkyl-carboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxy, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonyl-aminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₁, arylC₁-C₆alkyl-carbonyl-

amino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, or C₁-C₆alkyl-CONR₇R₈ wherein the alkyl and aryl groups are optionally substituted and R₁₁ is NR₉R₁₀, or C₁-C₆alkylNR₉R₁₀;

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R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted; or R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic cyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, the ring system can optionally be substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, C₁-C₆alkyloxy, arylC₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino-C₁-C₆alkyl or NR₉R₁₀, wherein R₉ and R₁₀ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted; or R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

with the proviso that when R₁ is COOH, R₂, R₃, R₄, R₅, and R₆ are H, n and m are 1, and X is S, then Y is not O, S, SO or SO₂;

when R₂, R₃, R₄, R₅, and R₆ are H, n and m are 1, X is S, and Y is O, then R₁ is not 5-tetrazol;

when R₁ is COOH, R₂, R₃, R₄, R₅, and R₆ are H, n and m are 1, X is S, and Y is O, then R₃ is not 5-tetrazol;

when R₁ is COOH, R₂, R₃, R₄, and R₆ are H, n and m are 1, X is S and Y is O, then R₅ is not 1-oxo-1,3-dihydro-isoindol-2-yl methyl, 1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl, ((4-oxo-chromene-4H-3-carbonyl)amino)methyl, 1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl, ((4-oxo-chromene-4H-3-carbonyl)amino)methyl, ((4-oxo-chromene-4H-2-carbonyl)amino)methyl, (3-furan-3-yl-acryloylomino)methyl, (3-furan-2-yl-acryloylamino)-methyl, ((3-oxo-indane-1-carbonyl)amino)methyl, 2,4-dioxo-thiazolidin-3-ylmethyl, 3,5-dimethoxy-benzoylamino-

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methyl, 5,6-dichloro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl, 1,3-dioxo-1,3,4,5,6,7-hexahydro-isoindol-2-ylmethyl, 1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl, (4-methoxy-benzenesulfonylamino)-methyl, 2-methyl-4-oxo-4H-quinazolin-3-ylmethyl, or 1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl;

when R₁ is COOH, R₂, R₃, R₄, and R₅ are H, n and m are 1, X is S, and Y is O, then R₆ is not 1,3,-dioxo-1,3-dihydro-isoindol-2-ylmethyl or acetylamino-methyl;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form.

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91. (Amended) A composition comprising an effective amount of a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

b3

93. (Amended) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 1 and an insulin sensitizer to said subject.

94. (Amended) A composition comprising an effective amount of a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

b4

96. (Amended) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound according to claim 1 and an agent stimulating insulin release from β cells.

b5

97. (Amended) A composition comprising a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

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99. (Amended) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 1 and an antiobesity agent.

Please add the following new claims:

100. (new) A composition according to claim 91, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

101. (new) A pharmaceutical composition according to claim 91, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

102. (new) A composition according to claim 91, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

103. (new) The method according to claim 93, wherein the insulin sensitizer is a thiazolidinedione or (-) 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

104. (new) The method according to claim 93, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione or (-) 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

105. (new) The method according to claim 93, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.